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Optimizing HF Outcomes Across the Spectrum: Emerging Evidence

Announcer:
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Dr. Desai:
Hi, this is CME on ReachMD, and I'm Dr. Akshay Desai.

Dr. McMurray:
Hi, I'm John McMurray.

Dr. Desai:
Our goal today in this brief session is to speak a little bit about the exciting new data and use of mineralocorticoid receptor antagonists in patients with heart failure, emphasizing data presented at the recent Heart Failure Society from the FINEARTS-HF trial.

And so to begin that conversation, John, since you led the trial, perhaps you could provide a little bit of context for the audience about what was done and what we learned.

Dr. McMurray:
We randomized just over 6,000 patients with heart failure and an ejection fraction of 40% or above, so patients with mildly reduced to preserve ejection fraction. To get into the trial, patients had to have symptomatic heart failure, to have structural heart disease, so in other words, an enlarged left atrium or left ventricular hypertrophy or both, a modest elevation in natriuretic peptides, and a need for diuretic therapy.

Patients were randomized to finerenone, a novel nonsteroidal mineralocorticoid receptor antagonist, so different than spironolactone and eplerenone, or matching placebo. And we had a primary endpoint that was a composite of total worsening heart failure events. So that's first or repeat worsening heart failure events. By worsening heart failure events, I mean an admission to hospital because of worsening heart failure or worsening heart failure treated in an outpatient setting but requiring intravenous therapy. And that was with cardiovascular death as the other component of the primary composite outcome.

We saw that there was a 16% relative risk reduction in the primary composite endpoint that was driven predominantly by the reduction in worsening heart failure events.There was an 18% reduction in worsening heart failure events.

And I think the other important finding in terms of efficacy was that we also saw an improvement in the Kansas City Cardiomyopathy Questionnaire total symptoms score patient-reported outcome.

And those benefits were seen with a very favorable safety profile.

Dr. Desai:
Can you tell us a little bit about the differences between finerenone as a nonsteroidal MRA and spironolactone or eplerenone, which are

the ones we have commercially available?

Dr. McMurray:
Finerenone is really the lead compound in this new class of nonsteroidal mineralocorticoid receptor antagonists. I think it genuinely is a new class because these drugs have a completely different chemical structure, and they also have different physiochemical properties, they have different tissue distribution, so we see, at least experimentally, more penetration in the myocardium, less effect on the kidney. So we think that they have a different profile balance of treatment effects in different tissues. We think also that they're less likely, certainly, than spironolactone to cause anti-androgen side effects such as gynecomastia and so on.

Dr. Desai:
And you presented a very interesting analysis of treatment by ejection fraction in FINEARTS-HF.

Dr. McMurray:
In fact, we saw that the ejection fraction did not modify the effect of finerenone at all. The benefit of finerenone seemed to be consistent across the whole spectrum of ejection fraction in the FINEARTS-HF trial.

I think, another very interesting analysis which had to do with something unique about FINEARTS, which was that we actually enrolled patients in hospital and shortly after discharge and, indeed, quite a high proportion of those patients, making FINEARTS different than our other trials in this type of patient population.

Dr. Desai:
We enrolled a patient population that included those in hospital or recently hospitalized in addition to those who were remote or had never been hospitalized.

We were able to see that in the over half of patients who had been enrolled proximate to a worsening heart failure event, say within 7 days or within 3 months of an event, the numerical reduction in the primary composite endpoint was actually even greater than in the residual population more remote from or without the worsening heart failure event. There was no statistical interaction between the time from the worsening heart failure event to randomization and the treatment effect, and by that, I mean statistically we could not identify a definitive time by treatment variation in the response.

But there is this signal that the benefit might be even more pronounced in those patients that are proximate to a heart failure event, and that has pretty important, I think, treatment implications because we know this population is at high risk.

Patients who are recently hospitalized or those with an ambulatory worsening heart failure event are at very high risk for subsequent mortality and readmission, and so if we had a treatment that was particularly effective, then this would fit very nicely in the evolving paradigm to utilize the hospitalization or the worsening event as an opportunity to intensify medical therapy.

Dr. McMurray:
So I think another important presentation publication at the Heart Failure Society was looking at patients on background treatment with SGLT2 inhibitors, which of course is our other strongly evidence-based treatment for this population. Do you want to summarize what we found in that population?

Dr. Desai:
We have now very well established data that SGLT2 inhibitors in particular and ARNIs in the subset of patients with mildly reduced ejection fraction, certainly those with ejection fraction below normal, are now encouraged in patients with heart failure and EF greater than 40%.

And so there's the question after FINEARTS, whether the benefits of finerenone are additive to those of established therapies. And I think that the examination of background therapy really suggests that, yes, indeed, addition of a nonsteroidal mineralocorticoid receptor antagonist finerenone is effective in this population regardless of background therapy. And I think the message, particularly about the additive benefit on top of SGLT2 inhibitors, was particularly important as it is for ARNI, because it begins to then help us understand a pathway to now guideline-directed medical therapy that is evolving for patients with heart failure and higher ejection fraction, as we have done in patients with the lower ejection fraction.

Dr. McMurray:
And maybe I'll just mention a couple of other presentations and publications at the Heart Failure Society that I think are maybe interrelated. So one was looking at the effects according to age, and we had patients over the age of 90 enrolled in FINEARTS, so we had the full spectrum of age. And I think it's terribly important that we always look at the effects of new treatment in older age groups, not just efficacy but also safety, and indeed, we've done that in great detail in FINEARTS. And I was delighted to see that the efficacy was

maintained across the full spectrum of age and, indeed, so was safety. So I thought that was a key additional finding.

And then, we, as I mentioned earlier, looked at the Kansas City Cardiomyopathy Questionnaires and patient-reported outcome, and we saw what, I think, perhaps superficially looks like a rather small 1.6-point improvement in KCCQ total symptom score overall, and that of course was significant but we've got to remember that that was in the population on average and indeed is very, very similar to what we've seen with other treatments, both in HFpEF and in HFrEF. And I think maybe for some particularly older patients, improving health status, improving quality of life, is a very important objective of treatment.

Dr. Desai:
I think as we close our brief review of FINEARTS here, I think it's also worth mentioning that all of this happened within a very short time of initiation of finerenone. We saw a time to clinical benefit that was within a couple of weeks of initiation of the drug for the first significant benefits for the primary composite. And so I think that this sort of, I think, begins to highlight finerenone as a really important option.

Any final closing comments about FINEARTS and the MRAs and heart failure?

Dr. McMurray:
I think the most important point to make is that we now have a second robust pillar of therapy for patients. In those people with an ejection fraction above 50% where we've previously had nothing until just a couple of years ago, now we've got SGLT2 inhibitors, now we've got finerenone. We're making progress. We can really begin to do something for these patients.

Dr. Desai:
Well, that's perfectly said. And I think that's all the time we have. I'd like to thank our listeners for tuning in and thank you, John, for joining me today. It was a pleasure to have this discussion about FINEARTS.

Dr. McMurray:
As always.

Announcer:
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